☐1: NP_570122. skeletal muscle a...[gi:18765707] BLink, Links

```
LOCUS       SKIP                     372 aa            linear   PRI 11-OCT-2002
DEFINITION  skeletal muscle and kidney enriched inositol phosphatase isoform 2;
            43-kDa form skeletal muscle and kidney enriched inositol
            phosphatase [Homo sapiens].
ACCESSION   NP_570122
VERSION     NP_570122.1  GI:18765707
DBSOURCE    REFSEQ: accession NM_130766.1
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 372)
  AUTHORS   Mitchell,C.A., Brown,S., Campbell,J.K., Munday,A.D. and Speed,C.J.
  TITLE     Regulation of second messengers by the inositol polyphosphate
            5-phosphatases
  JOURNAL   Biochem. Soc. Trans. 24 (4), 994-1000 (1996)
  MEDLINE   97123250
   PUBMED   8968499
REFERENCE   2  (residues 1 to 372)
  AUTHORS   Drayer,A.L., Pesesse,X., De Smedt,F., Communi,D., Moreau,C. and
            Erneux,C.
  TITLE     The family of inositol and phosphatidylinositol polyphosphate
            5-phosphatases
  JOURNAL   Biochem. Soc. Trans. 24 (4), 1001-1005 (1996)
  MEDLINE   97123251
   PUBMED   8968500
REFERENCE   3  (residues 1 to 372)
  AUTHORS   Ijuin,T., Mochizuki,Y., Fukami,K., Funaki,M., Asano,T. and
            Takenawa,T.
  TITLE     Identification and characterization of a novel inositol
            polyphosphate 5-phosphatase
  JOURNAL   J. Biol. Chem. 275 (15), 10870-10875 (2000)
  MEDLINE   20219123
   PUBMED   10753883
COMMENT     REVIEWED REFSEQ: This record has been curated by NCBI staff. The
            reference sequence was derived from AB036830.1.
            Summary: This gene encodes a protein with 5-phosphatase activity
            toward polyphosphate inositol. The protein localizes to the cytosol
            in regions lacking actin stress fibers. It is thought that this
            protein may negatively regulate the actin cytoskeleton. Alternative
            splicing of this gene results in two transcript variants encoding
            different isoforms.
            Transcript Variant: This variant (2) has an additional 229 nt exon
            in its 5' end, as compared to variant 1. Thus isoform 2 has a
            distinct N-terminus and is 76 aa shorter than isoform 1.
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                     /chromosome="17"
                     /map="17p13.3"
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                     phosphatase isoform 2"
                     /note="43-kDa form skeletal muscle and kidney enriched
                     inositol phosphatase"
     Region          9..248
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                     catalytic domain homologues"
                     /note="IPPc"
                     /db_xref="CDD:smart00128"
     Region          17..242
                     /region_name="Endonuclease/Exonuclease/phosphatase family.
                     This large family of proteins includes magnesium dependent
                     endonucleases and a large number of phosphatases involved
                     in intracellular signalling. This family includes: AP
                     endonuclease proteins EC:4.2.99.18, DNase I proteins
                     EC:3.1.21.1, Synaptojanin an inositol-1,4,5-trisphosphate
                     phosphatase EC:3.1.3.56, Sphingomyelinase EC:3.1.4.12 and
                     Nocturnin"
                     /note="Exo_endo_phos"
                     /db_xref="CDD:pfam03372"
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                     /allele="S"
                     /db_xref="dbSNP:3208368"
     CDS             1..372
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                     /coded_by="NM_130766.1:619..1737"
                     /db_xref="LocusID:51763"
ORIGIN
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       61 klygyyvsii nchlpphisn nyqrlehfdr ilemqncegr dipnildhdl iiwfgdmnfr
      121 iedfglhfvr esiknrcygg lwekdqlsia kkhdpllref qegrllfppt ykfdrnsndy
      181 dtsekkrkpa wtdrilwrlk rqpcagpdtp ippashfsls lrgysshmty gisdhkpvsg
      241 tfdlelkplv saplivlmpe dlwtvendmm vsysstsdfp sspwdwigly kvglrdvndy
      301 vsyawvgdsk vscsdnlnqv yidisniptt edefllcyys nslrsvvgis rpfqippgsl
      361 redplgeaqp qi
//
```

Revised: July 5, 2002.

**Query: gi|1399101 phosphatidylin sit l (4,5)bisphosphate 5-phosphatase homol g; has similarity to motifs conserved in phosphatidylin sitol (4,5)bisph sphate 5-phosphatases, Swiss-Prot Accession Number Q01968, and the product of GenBank Accession Number M74161**

## COG5411 assigned by Cognitor (3 best hits)

Best hits | Common Tree | Taxonomy Report | 3D structures | CDD-Search | GI list

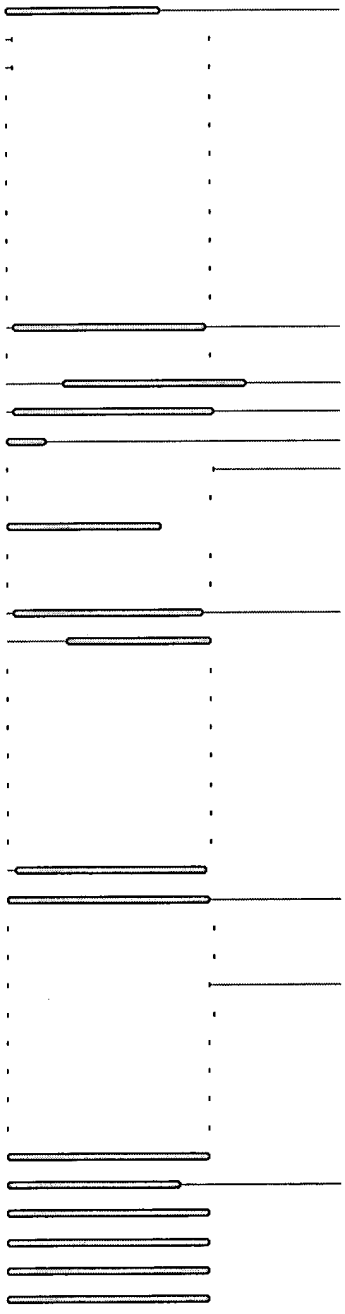
**153 BLAST hits to 19 unique species** Sort by taxonomy proximity

0 Archaea | 0 Bacteria | 105 Metazoa | 13 Fungi | 30 Plants | 0 Viruses | 5 Other Eukaryotae

Keep only [ ] Cut-Off [100] Select Reset

329 aa

| SCORE | P | ACCESSION | GI | PROTEIN DESCRIPTION |
|---|---|---|---|---|
| 1803 | 27 | BAA92341 | 7209857 | 43-kDa form skeletal muscle and kidne |
| 1803 | 27 | BAA92340 | 7209855 | skeletal muscle and kidney enriched : |
| 1791 | 27 | NP_570122 | 18765707 | skeletal muscle and kidney enriched : |
| 1791 | 27 | AAH04362 | 13279338 | SKIP for skeletal muscle and kidney e |
| 1313 | 21 | AAC60757 | 2121241 | putative phosphoinositide 5-phosphat |
| 732 | 21 | XP_137500 | 23620188 | phosphatidylinositol (4,5) bisphosph |
| 731 | 21 | BAA90553 | 6906704 | proline-rich inositol polyphosphate ! |
| 726 | 27 | BAC04657 | 21755308 | unnamed protein product [Homo sapien |
| 707 | 27 | AAD15618 | 4314432 | similar to phosphatidylinositol (4,5) |
| 649 | 27 | XP_038489 | 22068673 | similar to phosphatidylinositol (4,5) |
| 489 | 27 | AAB03216 | 1399105 | phosphatidylinositol (4,5)bisphosphat |
| 423 | 8 | AAF48627 | 7293245 | CG9784-PA [Drosophila melanogaster] |
| 409 | 8 | EAA00417 | 21288096 | agCP9655 [Anopheles gambiae str. PES |
| 406 | 27 | XP_171903 | 22066542 | similar to skeletal muscle and kidney |
| 354 | 8 | AAF57919 | 7302845 | CG6805-PA [Drosophila melanogaster] |
| 352 | 27 | XP_170949 | 22045277 | similar to Type II inositol-1,4,5-tr |
| 352 | 27 | AAA79207 | 1019103 | inositol polyphosphate 5-phosphatase |
| 338 | 21 | BAB23505 | 12836107 | data source:MGD, source key:MGI:1032 |
| 338 | 21 | AAB95412 | 9945302 | inositol polyphosphate 5-phosphatase |
| 338 | 21 | AAH28864 | 20809342 | Unknown (protein for MGC:25218) [Mus |
| 338 | 21 | AAG23293 | 15418718 | inositol polyphosphate 5-phosphatase |
| 330 | 8 | EAA09938 | 21297793 | agCP11786 [Anopheles gambiae str. PE |
| 324 | 21 | T42384 | 7513696 | inositol-1,4,5-trisphosphate 5-phosp |
| 282 | 27 | NP_001578 | 13325070 | phosphatidylinositol polyphosphate 5- |
| 282 | 27 | AAB03839 | 13254464 | ocrl1 [Homo sapiens] |
| 282 | 27 | CAA18150 | 3171882 | dJ454M7.1.2 (Lowe Oculocerebrorenal |
| 282 | 27 | CAA18151 | 4160528 | dJ454M7.1.1 (Lowe Oculocerebrorenal |
| 282 | 27 | 1814461A | 228953 | OCRL-1 gene |
| 282 | 27 | AAA59964 | 13249985 | Lowe oculocerebrorenal syndrome prot |
| 282 | 27 | Q01968 | 12644378 | Inositol polyphosphate 5-phosphatase |
| 272 | 8 | EAA00566 | 21288245 | agCP9746 [Anopheles gambiae str. PES |
| 270 | 7 | AAG18574 | 10567757 | synaptojanin UNC-26A [Caenorhabditis |
| 270 | 7 | AAG18575 | 10567759 | synaptojanin UNC-26B [Caenorhabditis |
| 268 | 8 | CAA15931 | 2749755 | /prediction=(method:''genefinder'', |
| 267 | 12 | AAG02341 | 9937209 | synaptojanin 1 [Lampetra fluviatilis] |
| 266 | 4 | CAD11414 | 16944690 | conserved hypothetical protein [Neur |
| 266 | 3 | CAB41466 | 4688596 | inositol 1,4,5-trisphosphate 5-phosp |
| 265 | 3 | AAD46036 | 5668810 | Contains similarity to gb\|M74161 ino |
| 264 | 21 | AAC40143 | 3241989 | synaptojanin 2 isoform epsilon [Mus |



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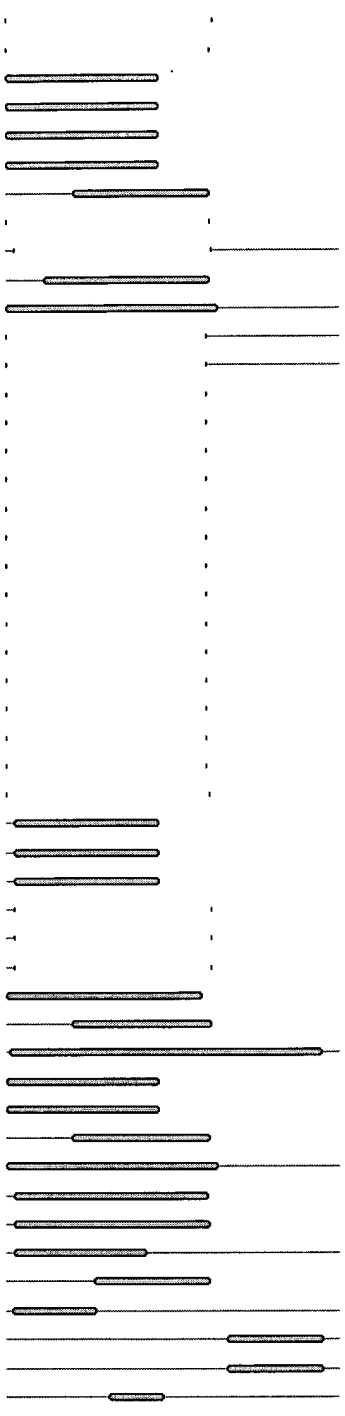
|---|---|---|---|---|
| 264 | 21 | AAC40146 | 3241995 | synaptojanin 2 isoform alpha [Mus mus |
| 264 | 21 | XP_110262 | 20348625 | expressed sequence AI481647 [Mus musc |
| 264 | 21 | BAB31837 | 12860016 | data source:MGD, source key:MGI:1201 |
| 264 | 21 | AAC40141 | 3241985 | synaptojanin 2 isoform beta [Mus musc |
| 264 | 21 | AAC40142 | 3241987 | synaptojanin 2 isoform delta [Mus mus |
| 260 | 27 | BAA74933 | 20521692 | KIAA0910 protein [Homo sapiens] |
| 260 | 21 | Q62910 | 8134729 | Synaptojanin 1 (Synaptic inositol-1, |
| 260 | 21 | 2204390A | 1586823 | synaptojanin |
| 260 | 21 | S68448 | 7514092 | synaptojanin, 170K - rat |
| 260 | 27 | AAC51921 | 2702321 | synaptojanin [Homo sapiens] |
| 260 | 21 | CAA07267 | 3367736 | DeltaSAC-synaptojanin1 [Rattus norve |
| 260 | 21 | | 26006227 | |
| 260 | 27 | AAC51922 | 2702323 | synaptojanin [Homo sapiens] |
| 260 | 21 | AAB60525 | 1166575 | synaptojanin |
| 258 | 3 | NP_172038 | 15220522 | hypothetical protein; protein id: At |
| 258 | 3 | AAF79735 | 8778727 | T25N20.12 [Arabidopsis thaliana] |
| 258 | 21 | AAK61723 | 16647986 | synaptojanin 2B2 [Rattus norvegicus] |
| 258 | 21 | AAK61722 | 16647984 | synaptojanin 2B1 [Rattus norvegicus] |
| 258 | 21 | AAB92481 | 2708493 | synaptojanin II [Rattus norvegicus] |
| 258 | 3 | AAC98062 | 4056496 | unknown protein [Arabidopsis thalian |
| 258 | 3 | AAC23399 | 3212848 | putative inositol polyphosphate 5'-p |
| 258 | 21 | AAC40144 | 3241991 | synaptojanin 2 isoform gamma [Mus mus |
| 258 | 21 | AAC33137 | 3478621 | synaptojanin 2 [Mus musculus] |
| 257 | 8 | AAF46796 | 7291368 | CG6562-PA [Drosophila melanogaster] |
| 257 | 8 | AAM52040 | 21464474 | SD04710p [Drosophila melanogaster] |
| 257 | 21 | BAA21652 | 2285875 | synaptojanin [Bos taurus] |
| 257 | 27 | AAN73051 | 25361067 | synaptojanin 2A [Homo sapiens] |
| 257 | 21 | O18964 | 10720298 | Synaptojanin 1 (Synaptic inositol-1, |
| 257 | 27 | AAG46036 | 12034892 | synaptojanin 2 [Homo sapiens] |
| 257 | 27 | AAD02178 | 4104822 | synaptojanin 2B [Homo sapiens] |
| 250 | 3 | AAD30615 | 4836913 | Putative inositol 1,4,5-trisphosphat |
| 249 | 27 | A41075 | 106731 | inositol-1,4,5-trisphosphate 5-phosp |
| 248 | 7 | C88883 | 25396130 | protein JC8.10 [imported] - Caenorha |
| 243 | 7 | CAB02743 | 3874363 | Hypothetical protein C16C2.3 [Caenor |
| 243 | 27 | XP_170860 | 22066536 | similar to skeletal muscle and kidne |
| 240 | 3 | BAB90404 | 20161480 | putative inositol-1, 4, 5-trisphosph |
| 239 | 3 | AAD15403 | 4263717 | putative inositol polyphosphate 5'-p |
| 237 | 4 | CAA86201 | 557848 | orf, len: 946, CAI: 0.12, similar to |
| 234 | 8 | AAB08434 | 1546841 | apyrase [Rhodnius prolixus] |
| 232 | 3 | CAB86425 | 7523406 | inositol-1, 4, 5-trisphosphate 5-Pho |
| 231 | 3 | AAD32289 | 4887753 | putative inositol polyphosphate 5'-p |
| 230 | 3 | AAB60921 | 2190557 | F5I14.11 [Arabidopsis thaliana] |
| 226 | 4 | CAB11494 | 6942000 | putative Inositol polyphosphate phos |
| 226 | 4 | T39233 | 7492669 | probable Inositol polyphosphate phos |
| 225 | 4 | 1I9YA | 14277798 | Chain A, Crystal Structure Of Inosit |
| 225 | 4 | CAA17882 | 2956769 | phosphatidylinositol phosphate phosp |
| 224 | 4 | CAB54821 | 5830513 | putative inositol polyphosphate phos |
| 222 | 4 | CAA95982 | 1302022 | ORF YNL106c [Saccharomyces cerevisia |
| 222 | 4 | CAA90520 | 929847 | ORF N2160 [Saccharomyces cerevisiae] |
| 221 | 8 | AAF49933 | 7294594 | CG10426-PA [Drosophila melanogaster] |
| 221 | 27 | AAA96658 | 556192 | 51C protein |
| 221 | 3 | AAG12525 | 10086465 | Putative inositol polyphosphate 5-ph |
| 221 | 3 | NP_564437 | 18399139 | inositol polyphosphate 5-phosphatase |
| 221 | 27 | CAA74743 | 2653424 | inositol polyphosphate 5-phosphatase |
| 221 | 3 | AAG17824 | 10444261 | inositol polyphosphate 5-phosphatase |
| 219 | 21 | AAF28187 | 6760079 | SH2-containing inositol 5-phosphatas |
| 219 | 21 | XP_133640 | 20838758 | inositol polyphosphate phosphatase-1 |
| 219 | 21 | BAA81818 | 5263147 | SHIP-2 [Rattus norvegicus] |
| 219 | 21 | BAA82308 | 5381251 | SH2-containing inositol phosphatase |
| 218 | 3 | CAB59428 | 6117853 | inositol-1,4,5-trisphosphate 5-Phosp |
| 218 | 4 | CAA64029 | 1164954 | YOR3231w [Saccharomyces cerevisiae] |
| 218 | 3 | AAG17825 | 10444263 | inositol polyphosphate 5-phosphatase |
| 218 | 3 | AAD10829 | 4204697 | putative inositol polyphosphate 5-ph |
| 217 | 3 | CAA17144 | 2894610 | putative protein [Arabidopsis thalia |
| 217 | 3 | NP_567547 | 18415007 | putative protein; protein id: At4g18 |



| | | | | |
|---|---|---|---|---|
| 217 | 3 | AAD10828 | 4204695 | putative inositol polyphosphate 5-phc |
| 214 | 3 | BAB11520 | 10178037 | contains similarity to inositol polyp |
| 210 | 3 | AAF43224 | 7239498 | Contains similarity to the inositol-: |
| 210 | 3 | AAK82558 | 15081807 | At1g71710/F14O23_9 [Arabidopsis thal: |
| 210 | 3 | NP_565023 | 18409892 | RIBOSOMAL PROTEIN, putative; protein |
| 210 | 3 | AAG51823 | 12323727 | putative inositol polyphosphate phosp |
| 209 | 27 | CAA97842 | 1483513 | Lowe oculocerebrorenal syndrome (OCRI |
| 207 | 3 | AAD21781 | 4522008 | putative inositol polyphosphate-5-phc |
| 206 | 8 | EAA09392 | 21297247 | agCP15025 [Anopheles gambiae str. PE: |
| 202 | 8 | AAL29114 | 16769790 | LP11751p [Drosophila melanogaster] |
| 201 | 3 | BAA99519 | 9081780 | hypothetical protein [Oryza sativa (: |
| 200 | 21 | AAB40610 | 1777942 | inositol polyphosphate 5' phosphatase |
| 199 | 21 | AAF25823 | 6708167 | inositol phosphatase s-SHIP [Mus musc |
| 199 | 21 | AAF25824 | 6708169 | inositol phosphatase s-SHIPD183 [Mus |
| 199 | 21 | JC6118 | 7513819 | SH2-containing inositol phosphatase |
| 199 | 21 | AAF69143 | 7767531 | SH2-containing inositol 5-phosphatase |
| 199 | 21 | AAB18937 | 1209068 | SH2-containing inositol-phosphatase |
| 199 | 21 | AAC52606 | 1236991 | SH2 containing inositol-5-phosphatase |
| 199 | 21 | AAD37118 | 5001726 | SH2-containing inositol phosphatase |
| 198 | 27 | AAC50453 | 1245337 | signaling inositol polyphosphate 5 ph |
| 198 | 27 | AAC50454 | 1277082 | signaling inositol polyphosphate 5 ph |
| 198 | 27 | CAA67071 | 1495456 | inositol polyphosphate 5- phosphatase |
| 198 | 27 | AAB53573 | 1619914 | SH2-containing inositol 5-phosphatase |
| 198 | 27 | AAB49680 | 1888525 | SH2 containing inositol-5-phosphatase |
| 198 | 27 | AAD00081 | 4097285 | signaling inositol polyphosphate phos |
| 198 | 27 | XP_096169 | 20537935 | similar to signaling inositol polyphc |
| 196 | 21 | AAC53023 | 1255352 | SH2-containing inositol phosphatase : |
| 193 | 3 | BAB11645 | 10178171 | inositol-1, 4, 5-trisphosphate 5-phos |
| 190 | 7 | T19021 | 7511557 | probable inositol phosphatase T25B9.: |
| 190 | 7 | NP_501999 | 17542560 | Endonuclease Exonuclease phosphatase |
| 190 | 7 | CAA94327 | 24817271 | Hypothetical protein T25B9.10 [Caenor |
| 189 | 21 | AAF86957 | 9295353 | inositol polyphosphate 5-phosphatase |
| 182 | 27 | AAF81404 | 8925284 | phosphatidylinositol polyphosphate 5- |
| 181 | 21 | BAA82150 | 5360761 | pharbin [Rattus norvegicus] |
| 179 | 3 | CAC00457 | 15387732 | possible hypothetical 131.3 Kd prote: |
| 179 | 27 | AAB03215 | 1399103 | phosphatidylinositol (4,5) bisphospha |
| 169 | 7 | AAA27979 | 289660 | Hypothetical protein C50C3.7 [Caenorh |
| 168 | 3 | EAA22794 | 23491200 | Homo sapiens KIAA0910 protein-relatec |
| 162 | 3 | CAD50826 | 23498756 | hypothetical protein [Plasmodium falc |
| 160 | 8 | AAC28738 | 3388165 | salivary nitrophorin [Cimex lectular: |
| 143 | 4 | CAA99075 | 1419885 | ORF YOL065c [Saccharomyces cerevisiae |
| 139 | 3 | AAN35707 | 23496045 | hypothetical protein [Plasmodium falc |
| 136 | 4 | CAD25856 | 19069388 | putative INOSITOL POLYPHOSPHATE-5-PHC |
| 133 | 3 | EAA15481 | 23478376 | hypothetical protein [Plasmodium yoe: |
| 130 | 3 | BAB89826 | 20160888 | contains EST AU069284(C53872)~simila: |
| 124 | 21 | AAB95413 | 2766531 | inositol polyphosphate 5-phosphatase |
| 104 | 21 | XP_126663 | 20912903 | RIKEN cDNA 2410154J16 [Mus musculus] |
| 104 | 21 | BAB27200 | 12846522 | data source:SPTR, source key:Q13137, |
| 105 | 4 | CAD21299 | 18376182 | related to inositol polyphosphate 5-p |

(FILE 'HOME' ENTERED AT 12:51:54 ON 05 DEC 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 12:52:06 ON 05 DEC 2002

| | | |
|---|---|---|
| L1 | 2043 | S 5-PHOSPHATASE |
| L2 | 887 | S L1 AND PY<1997 |
| L3 | 387 | DUP REM L2 (500 DUPLICATES REMOVED) |
| L4 | 17 | S L3 AND (ANTIBODY OR ANTISERA OR POLYCLONAL) |
| L5 | 0 | S NUSSBAUM RL/AU |
| L6 | 6 | S NUSSBAUM/AU |
| L7 | 6 | DUP REM L6 (0 DUPLICATES REMOVED) |
| L8 | 103 | S NUSSBAUM R/AU |
| L9 | 69 | DUP REM L8 (34 DUPLICATES REMOVED) |
| L10 | 0 | S L9 AND L2 |
| L11 | 3 | S L9 AND L1 |

L4 ANSWER 1 OF 17 MEDLINE
ACCESSION NUMBER: 97094645 MEDLINE
DOCUMENT NUMBER: 97094645 PubMed ID: 8939879
TITLE: Regulation of phosphatidylinositol 3,4,5-trisphosphate **5'-phosphatase** activity by insulin.
AUTHOR: Guilherme A; Klarlund J K; Krystal G; Czech M P
CORPORATE SOURCE: Program in Molecular Medicine and Department of Biochemistry and Molecular Biology, University of Massachusetts Medical Center, Worcester, Massachusetts 01605, USA.
CONTRACT NUMBER: DK30648 (NIDDK)
DK30898 (NIDDK)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1996 Nov 22)** 271 (47) 29533-6.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 20000303
Entered Medline: 19970113

AB Polyphosphoinositides are thought to be mediators of cellular signaling pathways as well as regulators of cytoskeletal elements and membrane trafficking events. It has recently been demonstrated that a class of phosphatidylinositol (PI) 3,4,5-P3 **5'-phosphatases** contains SH2 domains and proline-rich regions, which are present in many signaling proteins. We report here that insulin stimulation of Chinese hamster ovary cells (CHO-T) expressing human insulin receptors causes an 8-10-fold increase in PI 3,4,5-P3 **5'-phosphatase** activity in anti-phosphotyrosine immunoprecipitates of the cell lysates. This insulin-sensitive polyphosphoinositide **5'-phosphatase** did not catalyze dephosphorylation of PI 4,5-P2. No change in **5'-phosphatase** activity was detected in insulin receptor or IRS-1 immune complexes in response to insulin. However, insulin treatment of CHO-T cells markedly increased the PI 3,4,5-P3 **5'-phosphatase** activity associated with Shc and Grb2. The insulin-regulated polyphosphoinositide **5'-phosphatase** was not immunoreactive with **antibody** raised against the recently cloned SHIP **5'-phosphatase** reported to associate with Shc and Grb2 in B lymphocytes. These data demonstrate that insulin causes formation of complexes containing a PI 3,4,5-P3 **5'-phosphatase**, and Shc or Grb2, or both, suggesting an important role of this enzyme in insulin signaling.

=> d ibib abs l4 2-17

L4 ANSWER 2 OF 17 MEDLINE
ACCESSION NUMBER: 96215347 MEDLINE
DOCUMENT NUMBER: 96215347 PubMed ID: 8626616
TITLE: Post-translational modification of human brain type I inositol-1,4,5-trisphosphate **5-phosphatase** by farnesylation.
AUTHOR: De Smedt F; Boom A; Pesesse X; Schiffmann S N; Erneux C
CORPORATE SOURCE: Interdisciplinary Research Institute, Universite Libre de Bruxelles, Campus Erasme, 1070 Brussels, Belgium.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1996 Apr 26)** 271 (17) 10419-24.

Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960708
Last Updated on STN: 19960708
Entered Medline: 19960621

AB In brain, type I inositol-1,4,5-trisphosphate **5-phosphatase** (InsP3 **5-phosphatase**) is the major isoenzyme hydrolyzing the calcium-mobilizing second messenger InsP3. Activity of this enzyme could be measured in both soluble and particulate fractions of tissue homogenates. The protein sequence showed a putative C-terminal isoprenylation site (CVVQ). In this study, two mutants have been generated. The first mutant (C409S) has a serine replacing a cysteine at position 409 of the wild-type enzyme. The second mutant (K407D1) is a deletion mutant that lacks the last five C-terminal amino acids. These constructs were individually expressed by transfection in COS-7 cells. Western blot analysis of wild-type transfected cells indicated that both soluble and particulate fractions had a 43-kDa immunoreactive band, with a higher proportion of the original homogenate associated with the particulate part. On the contrary, when the two mutated constructs were transfected in COS-7 cells, the phosphatase was predominantly soluble. Confocal immunofluorescence studies showed the wild-type enzyme to be present on the cell surface of transfected COS-7 cells and in subcellular compartments around the nucleus. This was not observed for the two mutants, where uniform immunofluorescence labeling was observed throughout the cytosol. Recombinant type I InsP3 **5-phosphatase** expressed in Escherichia coli was a substrate of purified farnesyltransferase. Altogether, the data therefore suggest a direct participation of Cys-409 in a C-terminally anchored InsP3 **5-phosphatase** by farnesylation.

L4 ANSWER 3 OF 17 MEDLINE
ACCESSION NUMBER: 96206042 MEDLINE
DOCUMENT NUMBER: 96206042 PubMed ID: 8654924
TITLE: p150Ship, a signal transduction molecule with inositol polyphosphate-**5-phosphatase** activity.
AUTHOR: Lioubin M N; Algate P A; Tsai S; Carlberg K; Aebersold A; Rohrschneider L R
CORPORATE SOURCE: Fred Hutchinson Cancer Research Center, Seattle, Washington 98104, USA.
CONTRACT NUMBER: CA20551 (NCI) CA40987 (NCI)
SOURCE: GENES AND DEVELOPMENT, **(1996 May 1)** 10 (9) 1084-95.
Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L36818; GENBANK-P32019; GENBANK-Q01968; GENBANK-U51742
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960808

Last Updated on STN: 20000303
Entered Medline: 19960726

AB The production, survival, and function of monocytes and macrophages is regulated by the macrophage colony-stimulating factor (M-CSF or CSF-1) through its tyrosine kinase receptor Fms. Binding of M-CSF to Fms induces the tyrosine phosphorylation and association of a 150-kD protein with the phosphotyrosine-binding (PTB) domain of Shc. We have cloned p150 using a modified yeast two-hybrid screen. p150 contains one SH2 domain, two potential PTB-binding sites, an ATP/GTP-binding domain, several potential SH3-binding sites, and a domain with homology to inositol polyphosphate-**5-phosphatases**. p150 **antibodies** detect this protein in FDC-P1 myeloid cells, but the same protein is not detectable in fibroblasts. The **antibodies** immunoprecipitate a 150-kD protein from quiescent or M-CSF-stimulated FDC-P1 cells that hydrolyzes PtdIns(3,4,5)P3, to PtdIns(3,4)P2. This activity is observed in Shc immunoprecipitates only after M-CSF stimulation. Retroviral expression of p150 in FD-Fms cells results in strong inhibition of cell growth in M-CSF and a lesser inhibition in IL-3. Ectopic expression of p150 in fibroblasts does not inhibit growth. This novel protein, p150(ship) (SH2-containing inositol phosphatase), identifies a component of a new growth factor-receptor signaling pathway in hematopoietic cells.

L4 ANSWER 4 OF 17 MEDLINE
ACCESSION NUMBER: 96096741 MEDLINE
DOCUMENT NUMBER: 96096741 PubMed ID: 8529643
TITLE: Tissue distribution and intracellular localisation of the 75-kDa inositol polyphosphate **5-phosphatase**.
AUTHOR: Speed C J; Matzaris M; Bird P I; Mitchell C A
CORPORATE SOURCE: Department of Medicine, Monash Medical School, Box Hill Hospital, Melbourne, Australia.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, **(1995 Nov 15)** 234 (1) 216-24.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960220
Last Updated on STN: 19960220
Entered Medline: 19960126

AB The 75-kDa inositol polyphosphate **5-phosphatase** (75-kDa **5-phosphatase**) hydrolyses several important mediators of intracellular calcium homeostasis, including inositol 1,4,5-trisphosphate [Ins(1,4,5)P3], inositol 1,3,4,5-tetrakisphosphate [Ins(1,3,4,5)P4] and phosphatidylinositol 4,5-bisphosphate [PtdIns(4,5)P2]. Northern analysis of various human tissues revealed the 75-kDa **5-phosphatase** has a ubiquitous expression, where differential splicing may occur in specific tissues. Prominent expression of a 4.4-kb transcript was noted in human lung, thymus, testes and placenta, and a 4.6-kb transcript was observed in heart, brain, kidney, ovary and colon. Determination of the intracellular location of the enzyme by indirect immunofluorescence, demonstrated that the 75-kDa **5-phosphatase** was associated with mitochondrial and cytosolic cellular compartments. Immunoprecipitation of the total cell homogenate of human lung carcinoma cells (A549) with anti-(recombinant 75-kDa **5-phosphatase**) **antibodies** revealed

that the 75-kDa **5-phosphatase** is the major PtdIns(4,5)P2 **5-phosphatase** in this cell line. Analysis of PtdIns(4,5)P2 **5-phosphatase** activity in subcellular fractions of A549 cells revealed peak 75-kDa **5-phosphatase** enzyme activity in the cytosolic and mitochondrial enriched fractions. Immunoblot analysis further confirmed the mitochondrial location of the enzyme. This study demonstrates the tissue distribution and intracellular location of the 75-kDa **5-phosphatase** and reveals a novel location for an enzyme involved in phosphatidylinositol turnover.

L4 ANSWER 5 OF 17 MEDLINE
ACCESSION NUMBER: 95236949 MEDLINE
DOCUMENT NUMBER: 95236949 PubMed ID: 7720525
TITLE: Pharmacokinetics and organ clearance of a 3'-biotinylated, internally [32P]-labeled phosphodiester oligodeoxynucleotide coupled to a neutral avidin/monoclonal **antibody** conjugate.
AUTHOR: Kang Y S; Boado R J; Pardridge W M
CORPORATE SOURCE: Department of Medicine, UCLA School of Medicine 90024.
CONTRACT NUMBER: R01-AI-28760 (NIAID)
SOURCE: DRUG METABOLISM AND DISPOSITION, **(1995 Jan)** 23 (1) 55-9.
Journal code: 9421550. ISSN: 0090-9556.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950605
Last Updated on STN: 19970203
Entered Medline: 19950523

AB The pharmacokinetics and organ uptake of a 3'-biotinylated, [32P] internally labeled 36-mer phosphodiester oligodeoxynucleotide (PO-ODN) were measured after intravenous injection in the anesthetized adult rat. The PO-ODN was antisense to the tat gene of the human immunodeficiency virus, and was 3'-biotinylated to a) protect against serum and tissue 3'-exonuclease activity, and b) facilitate coupling to a neutral avidin-based transcellular drug delivery vector. The latter was comprised of a covalent conjugate of neutral avidin (NLA) and the OX26 murine monoclonal **antibody** to the rat transferrin receptor. The PO-ODN was internally labeled at the 21-nucleotide position to prevent rapid hydrolysis [32P] label by serum and tissue **5'-phosphatases**. The uptake of the 3'-bio-[32P21]PO-ODN by brain, heart, kidney, lung, and liver was measured. The studies show that the unconjugated 3'-bio-[32P21]PO-ODN was rapidly removed from plasma, with a mean residence time of 22 +/- 1 min and a systemic clearance of 9.2 +/- 0.5 ml/min/kg. Large amounts of [32P] radioactivity were recovered in the urine following the injection of the PO-ODN, and when this fraction was included in the calculation of the renal clearance parameter, the renal clearance was 20-fold higher, indicating the principal site of organ clearance of the unconjugated PO-ODN was the kidney. Conjugation of the 3'-bio-PO-ODN to the NLA-OX26 vector reduced the systemic clearance 50%, owing to a > 10-fold reduction in renal clearance. Following conjugation of the 3'-bio-PO-ODN to the NLA-OX26 vector, the major clearance organ was the liver.(ABSTRACT TRUNCATED AT 250 WORDS)

L4 ANSWER 6 OF 17 MEDLINE

ACCESSION NUMBER: 94230317 MEDLINE
DOCUMENT NUMBER: 94230317 PubMed ID: 8175661
TITLE: Adriamycin inhibits inositol 1,4,5-trisphosphate 3-kinase activity in vitro and blocks formation of inositol 1,3,4,5-tetrakisphosphate in stimulated Jurkat T-lymphocytes. Does inositol 1,3,4,5-tetrakisphosphate play a role in Ca(2+)-entry?.
AUTHOR: da Silva C P; Emmrich F; Guse A H
CORPORATE SOURCE: Max Planck Society, Clinical Research Unit for Rheumatology/Immunology, Institute for Clinical Immunology of the University, Erlangen, Germany.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1994 Apr 29)** 269 (17) 12521-6.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940620
Last Updated on STN: 19970203
Entered Medline: 19940606

AB Effects of the cytostatic drug adriamycin on inositol polyphosphate metabolism were analyzed in a human T-cell line (Jurkat) using a recently developed anion-exchange high performance liquid chromatography/post-column complexometric dye system. Treatment of intact T-cells with adriamycin prior to stimulation with an anti-CD3 monoclonal **antibody** induced a dose- and time-dependent decrease in the intracellular level of inositol 1,3,4,5-tetrakisphosphate (complete inhibition after 2 h at 10 microM adriamycin) and an increase in the level of inositol 1,3,4-trisphosphate without significantly changing the levels of other inositol phosphates. A marked inhibition of the inositol 1,4,5-trisphosphate 3-kinase activity and a slight activation of the inositol 1,3,4,5-tetrakisphosphate **5-phosphatase** activity were observed in cytosolic extracts in the presence of adriamycin, providing an explanation for the drug-induced metabolic effect. Adriamycin thus seems to be an extremely valuable tool for further dissecting inositol polyphosphate metabolism, as well as signaling pathways. Along these lines, we observed that adriamycin did not change the free cytosolic Ca2+ concentration of Jurkat T-lymphocytes and, in particular, did not modulate Ca2+ influx upon T-cell receptor stimulation.

We conclude that (i) inositol phosphate signaling pathways constitute an as yet undescribed target for the action of adriamycin and that (ii) an increase of inositol 1,3,4,5-tetrakisphosphate is not necessary for sustained Ca(2+)-entry in stimulated T-cells.

L4 ANSWER 7 OF 17 MEDLINE
ACCESSION NUMBER: 94148835 MEDLINE
DOCUMENT NUMBER: 94148835 PubMed ID: 7508913
TITLE: Purification of two immunologically related phosphatidylinositol-(4,5)- bisphosphate phosphatases from bovine brain cytosol.
AUTHOR: Palmer F B; Theolis R Jr; Cook H W; Byers D M
CORPORATE SOURCE: Atlantic Research Centre, Halifax, Nova Scotia.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1994 Feb 4)** 269 (5) 3403-10.

Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940330
Last Updated on STN: 19970203
Entered Medline: 19940318

AB Two phosphatidylinositol-(4,5)-bisphosphate (PtdIns-(4,5)P2) phosphatase activities were isolated from a 45% saturated (NH4)2SO4 fraction of the soluble cytosol (100,000 x g supernatant) of bovine cerebral hemispheres by ion-exchange chromatography on Q-Sepharose (Q-1 and Q-2). Each was further purified on heparin-Sepharose, butyl-agarose, and/or Cibacron blue F3GA to yield products of similar specific activity (70-100 mumol/min/mg protein, 1000-2000-fold purification). Salt was required to stabilize activity and dithiothreitol was required to preserve maximum activity and to prevent or reverse aggregation that resisted disruption by mercaptoethanol and/or SDS. Monoclonal **antibodies** were prepared that recognized several components in the partially purified preparations.

Immunoabsorption of activity by monoclonal **antibodies** that had been chemically cross-linked to protein A-Sepharose followed by SDS-polyacrylamide gel electrophoresis of absorbed proteins was used to identify the active components as a 155-kDa protein in Q-1 and a 115-kDa protein in Q-2. Two **antibodies** recognized different epitopes in the 155-kDa phosphatase. A third **antibody** recognized a common epitope in both phosphatases indicating that the two enzymes are related. Both phosphatases were Mg(2+)-dependent, exhibited similar kinetic properties, and hydrolyzed PtdIns(4,5)P2 but not PtdIns(4)P, phosphatidic acid, or several other phosphate monoesters. They hydrolyzed inositol (1,4,5)-trisphosphate at 30% of the rate with PtdIns(4,5)P2 and this activity co-purified with PtdIns(4,5)P2 phosphatase activity. High molecular weight PtdIns(4,5)P2 phosphatases may be precursors of lower molecular weight soluble Type II inositol polyphosphate-**5-phosphatases** shown to account for the PtdIns(4,5)P2 phosphatase activity in platelets (Matzaris, M., Jackson, S.P., Laxminarayan, M., Speed, C.J., and Mitchell, C.A. (1994) J. Biol. Chem. 269, 3397-3402). The three **antibodies** did not inhibit activity but recognized both native and denatured (Western blots) phosphatases and should be useful tools to study the distribution, structure, and regulation of the two forms of PtdIns(4,5)P2 phosphatase.

L4 ANSWER 8 OF 17 MEDLINE
ACCESSION NUMBER: 94148834 MEDLINE
DOCUMENT NUMBER: 94148834 PubMed ID: 8106379
TITLE: Identification and characterization of the phosphatidylinositol-(4, 5)-bisphosphate **5-phosphatase** in human platelets.
AUTHOR: Matzaris M; Jackson S P; Laxminarayan K M; Speed C J; Mitchell C A
CORPORATE SOURCE: Department of Medicine, Monash Medical School, Box Hill Hospital, Melbourne, Australia.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1994 Feb 4)** 269 (5) 3397-402.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940330
Last Updated on STN: 19970203
Entered Medline: 19940318

AB Phosphatidylinositol (4,5)-bisphosphate (PtdIns(4,5)-P2) is the precursor of several second messenger molecules. In unstimulated cells PtdIns(4,5)P2 is hydrolyzed by a PtdIns(4,5)P2 **5-phosphatase** to form phosphatidylinositol 4-phosphate (PtdIns(4)P) which is subsequently recycled to phosphatidylinositol. PtdIns(4,5)P2 **5-phosphatase** activity was detected in platelet cytosolic and particulate fractions. The platelet PtdIns(4,5)P2 **5-phosphatase** activity was magnesium but not calcium dependent. The elution profile of platelet cytosolic PtdIns(4,5)P2 **5-phosphatase** from anion exchange resins, exactly matched that of the 75-kDa inositol-polyphosphate **5-phosphatase** (Ins(1,4,5)P3 **5-phosphatase**). The latter is a signal terminating enzyme responsible for the hydrolysis of inositol (1,4,5)-trisphosphate (Ins(1,4,5)P3) to inositol (1,4)-bisphosphate (Mitchell, C.A., Connolly, T.M., and Majerus, P.W. (1989) J. Biol. Chem. 264, 8873-8877). **Polyclonal antibodies** raised against recombinant 75-kDa Ins(1,4,5)P3 **5-phosphatase** specifically immunoprecipitated all PtdIns-(4,5)P2 **5-phosphatase** activity from both the platelet membrane and cytosolic fractions. Purified 75-kDa Ins(1,4,5)P3 **5-phosphatase** hydrolyzed PtdIns(4,5)P2 forming PtdIns(4)P (Km = 250 microM). By contrast, purified membrane-associated 43-kDa Ins(1,4,5)P3 **5-phosphatase** did not hydrolyze PtdIns(4,5)P2. In the unstimulated platelet, recycling of PtdIns-(4,5)P2 to PtdIns(4)P is mediated by the 75-kDa Ins-(1,4,5)P3 **5-phosphatase**.

L4 ANSWER 9 OF 17 MEDLINE
ACCESSION NUMBER: 94117443 MEDLINE
DOCUMENT NUMBER: 94117443 PubMed ID: 8288593
TITLE: Purple acid phosphatase of the human macrophage and osteoclast. Characterization, molecular properties, and crystallization of the recombinant di-iron-oxo protein secreted by baculovirus-infected insect cells.
AUTHOR: Hayman A R; Cox T M
CORPORATE SOURCE: Department of Medicine, University of Cambridge, Addenbrooke's Hospital, United Kingdom.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1994 Jan 14)** 269 (2) 1294-300.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 19940312
Last Updated on STN: 19940312
Entered Medline: 19940222

AB The purple phosphatases catalyze hydrolysis of phosphate esters (optimum pH approximately 5) and are resistant to inhibition by dextro-rotatory tartrate; their distinctive color is due to Fe(III)-phenolate charge-transfer transitions at their active site. Expression of human purple phosphatase, designated type 5 acid phosphatase, is restricted to osteoclasts and other activated cells of monohistiocytic lineage, but its

biological role in relation to bone resorption and phagocytosis is unknown. To characterize this enzyme further, we have engineered the human type 5 acid phosphatase into a baculovirus vector expression system that enabled milligram quantities of purple protein to be purified from medium containing Sf9 host cells. The phosphatase cDNA was transcribed as a single RNA species of 1.5 kilobases as in human tissues. Tartrate-resistant acid phosphatase activity reacting with uteroferrin **antisera** appeared in the culture medium, from which up to 8 mg/liter was purified by two-step cation-exchange chromatography at pH 8.0. Two isoforms of approximately 36 kDa were identified by SDS-polyacrylamide electrophoresis and were converted to a single species of apparent molecular size 34 kDa upon treatment with N-glycosidase F, indicating secreted glycoforms of a single polypeptide. Mass spectroscopy showed that the mean molecular mass of the active, secreted glycoprotein was 35849 Da. The recombinant enzyme (specific activity, 190 mumol p-nitrophenol/min/mg at 37 degrees C) contained 2 iron atoms/molecule and formed purple, monoclinic crystals. Exposure to the ferric chelator, 1,2-dimethyl-3-hydroxypyrid-4-one, rapidly inactivated the enzyme, which was not inhibited by alpha, alpha'-bipyridyl, a ferrous chelator. That ferric iron is essential for enzymatic catalysis, was further indicated by the synergistic effects of the reductant, dithiothreitol, and bipyridyl on phosphatase activity. The recombinant purple phosphatase catalyzed the peroxidation of 5-aminophthalhydrazide (luminol), as evidenced by the induction of chemiluminescence; this reaction was inhibited by alpha, alpha'-bipyridyl at concentrations that did not inhibit phosphatase activity. The divalent iron moiety of human type **5 phosphatase** may therefore participate in the generation of free radical species by fluid-phase reactions involving Fenton chemistry that are dissociated from its phosphatase function.

L4 ANSWER 10 OF 17 MEDLINE
ACCESSION NUMBER: 93222738 MEDLINE
DOCUMENT NUMBER: 93222738 PubMed ID: 8385519
TITLE: Lectins and anti-T monoclonal **antibodies**-induced changes of second messengers generating enzymes in human peripheral blood mononuclear cells.
AUTHOR: Graber R; Leoni L; Carrel S; Losa G A
CORPORATE SOURCE: Laboratorio di Patologia Cellulare, Istituto Cantonale di Patologia, Locarno, Switzerland.
SOURCE: CELLULAR AND MOLECULAR BIOLOGY, **(1993 Feb)** 39 (1) 45-54.
Journal code: 9216789. ISSN: 0145-5680.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930521
Last Updated on STN: 20000327
Entered Medline: 19930507

AB A five min. incubation of peripheral blood mononuclear cells (PBMN) with either phytohaemagglutinin (PHA) or concanavalin A (ConA) resulted in distinct subcellular redistribution patterns of phosphatidylinositol 4,5-bisphosphate phospholipase C [PtdIns(4,5)P2-PLC] and myo-inositol 1,4,5-trisphosphate monophosphatase [Ins(1,4,5)P3-monophosphatase] activities. When compared to control cells, PHA-treated PBMN cells displayed a significant increase of PtdIns(4,5)P2-PLC and

Ins(1,4,5)P3-monophosphatase relative specific activities in the nuclear fraction along with an increment (D) in enzyme amount of 6.5% and 7.3%, respectively. Incubation with B66.6, an anti-CD4 monoclonal **antibody** (Mab) which specifically activates CD4(+)-T cells in the absence of any other stimuli, also induced changes of these activities in the nuclear fraction, thus mimicking the effect of PHA observed in helper T cell subpopulation. No changes were detected after incubation of PBMN cells with the non mitogenic anti-CD4 MAb 101-69, or with an anti-CD3 MAb which activates T cells only in the presence of a second stimulus. On the other hand, after incubation with ConA, PtdIns(4,5)P2-PLC relative specific activity was enhanced in the microsomal fraction while the Ins(1,4,5)P3-monophosphatase activity increased in both nuclear and microsomal fractions and decreased in cytosol. An increment D of 4.6% and 10.9% for PtdIns(4,5)P2-PLC and Ins(1,4,5)P3-monophosphatase, respectively, was measured in the microsomal fraction. Only after three days of incubation with a mitogenic anti-CD2 MAb Lau-2.1.2, the PtdIns(4,5)P2-PLC activity increased in the particulate fraction of PBMN similar to ConA treatment.

L4 ANSWER 11 OF 17 MEDLINE
ACCESSION NUMBER: 93186806 MEDLINE
DOCUMENT NUMBER: 93186806 PubMed ID: 8383126
TITLE: Purification and characterization of a 43-kDa membrane-associated inositol polyphosphate **5-phosphatase** from human placenta.
AUTHOR: Laxminarayan K M; Matzaris M; Speed C J; Mitchell C A
CORPORATE SOURCE: Department of Medicine, Monash Medical School, Box Hill Hospital, Melbourne, Australia.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1993 Mar 5)** 268 (7) 4968-74.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930416
Last Updated on STN: 19930416
Entered Medline: 19930406

AB We have identified, isolated, and characterized a membrane-associated inositol polyphosphate **5-phosphatase** (**5-phosphatase**) from the particulate fraction of human placenta. The enzyme was purified 3700-fold from a detergent extract of human placental membranes to apparent homogeneity, by chromatography on DEAE-Sepharose, S-Sepharose, hydroxylapatite, and Biosil SEC 250 HPLC gel filtration. The purified **5-phosphatase** has a molecular mass of 43 kDa as determined by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and gel filtration chromatography. The enzyme hydrolyzes inositol 1,4,5-trisphosphate (Ins(1,4,5)P3) to inositol 1,4 bisphosphate (Ins(1,4)P2) with an apparent Km of 5 microM. The 43-kDa **5-phosphatase** also hydrolyzes inositol 1,3,4,5-tetrakisphosphate (Ins(1,3,4,5)P4) with an apparent Km of 1.2 microM. The enzyme requires Mg2+ ions for activity and is inhibited by Ca2+ concentrations greater than 100 microM. **Polyclonal antibodies** developed against the membrane-associated enzyme immunoprecipitate the purified membrane-associated placental **5-phosphatase** and the platelet Type I cytosolic enzyme, but not the 75-kDa platelet Type II **5-phosphatase**. These results demonstrate that the purified membrane **5-phosphatase** bears physical and

immunological similarity with the Type I cytosolic platelet enzyme.

L4 ANSWER 12 OF 17 MEDLINE
ACCESSION NUMBER: 92041857 MEDLINE
DOCUMENT NUMBER: 92041857 PubMed ID: 1718960
TITLE: Cloning and expression of human 75-kDa inositol polyphosphate-**5-phosphatase**.
AUTHOR: Ross T S; Jefferson A B; Mitchell C A; Majerus P W
CORPORATE SOURCE: Washington University School of Medicine, Division of Hematology-Oncology, St. Louis, Missouri 63110.
CONTRACT NUMBER: HLBI-14147 (NHLBI)
HLBI-16634 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1991 Oct 25)** 266 (30) 20283-9.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-M74161; GENBANK-S60729; GENBANK-S61326; GENBANK-S61330; GENBANK-S61332; GENBANK-S61335; GENBANK-S61337; GENBANK-S61340; GENBANK-S61342; GENBANK-S61344
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19960129
Entered Medline: 19911202

AB Inositol polyphosphate-**5-phosphatase** (**5-phosphatase**) hydrolyzes inositol 1,4,5-trisphosphate and inositol 1,3,4,5-tetrakisphosphate and thereby functions as a signal terminating enzyme in cellular calcium ion mobilization. A cDNA encoding human platelet **5-phosphatase** has been isolated by screening for beta-galactosidase fusion proteins that bind to inositol 1,3,4,5-tetrakisphosphate. The sensitivity of the screening procedure was enhanced 50- to 100-fold by amplification of "sublibraries" prior to carrying out binding assays. The sequences derived from the "expression clone" were used to screen human erythroleukemia cell line and human megakaryocytic cell line cDNA libraries. We obtained two additional clones which together consist of 2381 base pairs. The amino-terminal amino acid sequence from the 75-kDa **5-phosphatase** purified from platelets is identical to amino acids 38-56 predicted from the cDNA. This suggests that the platelet **5-phosphatase** is formed by proteolytic processing of a larger precursor. The cDNA predicts that the mature enzyme contains 635 amino acids (Mr 72, 891). **Antibodies** directed against recombinant TrpE fusion proteins of either an amino-terminal region or a carboxyl-terminal region immunoprecipitate the enzyme activity from a preparation of the 75-kDa form of platelet **5-phosphatase** (Type II) but do not precipitate the distinct 47-kDa **5-phosphatase** (Type I) also found in platelets. In addition, the recombinant protein expressed in Cos-7 cells has the same **5-phosphatase** activity as the platelet **5-phosphatase**.

L4 ANSWER 13 OF 17 MEDLINE
ACCESSION NUMBER: 91182529 MEDLINE
DOCUMENT NUMBER: 91182529 PubMed ID: 1706930
TITLE: Soluble and particulate inositol 1,4,5-trisphosphate **5-phosphatases** show common antigenic determinants.

AUTHOR: Verjans B; Hollande F; Moreau C; Lejeune C; Erneux C
CORPORATE SOURCE: Institut de Recherche Interdisciplinaire (IRIBHN), Universite Libre de Bruxelles, Brussels, Belgium.
SOURCE: CELLULAR SIGNALLING, **(1990)** 2 (6) 595-9.
Journal code: 8904683. ISSN: 0898-6568.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910526
Last Updated on STN: 19960129
Entered Medline: 19910506

AB Inositol 1,4,5-trisphosphate **5-phosphatase** catalyses the dephosphorylation of the phosphate in the 5-position from inositol 1,4,5-trisphosphate and inositol 1,3,4,5-tetrakisphosphate. One particulate and two soluble enzymes were previously described in bovine brain. In this study, we have obtained a precipitating antiserum against soluble type I inositol 1,4,5-trisphosphate **5-phosphatase**. The particulate, but not the soluble type II enzyme, was immunoprecipitated by the serum. Inositol 1,4,5-trisphosphate **5-phosphatase** activity from crude extracts of rat brain, human platelets and rat liver were immunoprecipitated by the same **antibodies**, suggesting the existence of common antigenic determinant among inositol 1,4,5-trisphosphate **5-phosphatases** of diverse sources.

L4 ANSWER 14 OF 17 MEDLINE
ACCESSION NUMBER: 90262548 MEDLINE
DOCUMENT NUMBER: 90262548 PubMed ID: 1693074
TITLE: Rat brain inositol 1,4,5-trisphosphate 3-kinase. Ca2(+)-sensitivity, purification and **antibody** production.
AUTHOR: Takazawa K; Lemos M; Delvaux A; Lejeune C; Dumont J E; Erneux C
CORPORATE SOURCE: Institute of Interdisciplinary Research, School of Medicine, Free University of Brussels, Campus Erasme, Belgium.
SOURCE: BIOCHEMICAL JOURNAL, **(1990 May 15)** 268 (1) 213-7.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
ENTRY DATE: Entered STN: 19900720
Last Updated on STN: 19970203
Entered Medline: 19900628

AB Inositol 1,4,5-trisphosphate (InsP3) 3-kinase catalyses the ATP-dependent phosphorylation of InsP3 to inositol 1,3,4,5-tetrakisphosphate (InsP4). InsP3 3-kinase was purified from rat brain by Blue-Sepharose, phosphocellulose and calmodulin (CaM)-Sepharose affinity chromatography. The purified enzyme was stimulated by Ca2+/CaM by 3-6-fold as compared with the activity measured in the presence of EGTA. Rat brain InsP3 3-kinase activity was associated with two silver-stained bands of about equal activity which migrated with an apparent Mr of 50,000 on SDS/polyacrylamide gels. InsP3 3-kinase activity from rat brain could be immunoprecipitated by an antiserum against the SDS/PAGE-purified 50,000-Mr protein doublet. InsP3 kinase activity from bovine brain and the InsP3

**5-phosphatase** activity from rat brain were not immunoprecipitated. On Western blot, the human brain crude InsP3 3-kinase reacted specifically, but less strongly than the rat brain enzyme, with the antiserum.

L4 ANSWER 15 OF 17 MEDLINE
ACCESSION NUMBER: 90219128 MEDLINE
DOCUMENT NUMBER: 90219128 PubMed ID: 1691309
TITLE: Alzheimer disease proteins (A68) share epitopes with tau but show distinct biochemical properties.
AUTHOR: Ksiezak-Reding H; Binder L I; Yen S H
CORPORATE SOURCE: Department of Pathology, Albert Einstein College of Medicine, Bronx, New York 10461.
SOURCE: JOURNAL OF NEUROSCIENCE RESEARCH, **(1990 Mar)** 25 (3) 420-30.
Journal code: 7600111. ISSN: 0360-4012.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900622
Last Updated on STN: 19980206
Entered Medline: 19900524

AB Alz 50, a monoclonal **antibody** raised against Alzheimer brain homogenate, reacts with neurofibrillary tangles, microtubule-associated proteins tau, and Alzheimer brain proteins of molecular weight 70-60 kDa (A68). To study the relationship between A68 and normal human tau we compared the biochemical properties of these proteins and tested the reactivity of A68 with eight **antibodies** (Alz 50, Tau 60, Tau-2, Tau 14, Tau-1, Ab 636.7, NP14, Tau 46) that bind to various regions of tau molecule. On Western blots, all tau-reactive **antibodies**, except Tau-1, recognized A68. Pretreatment with alkaline phosphatase was required for the Tau-1 binding to A68. A68 consisted of three polypeptides of 68, 64, and 60 kDa, while tau contained 4-6 polypeptides of 50-65 kDa. A68 was less heterogenous than tau in the number of pI variants on two-dimensional gels. All A68 variants were more acidic (pI 5.5-6.5) than human tau (pI 6.5-8.5). **Phosphatase** treatment had only a minor effect on the pI and mobility of A68. Limited proteolysis of A68 with trypsin or chymotrypsin generated large fragments of 56-66 kDa (chymotrypsin) and 40-45 kDa (trypsin). While none of the fragments was recognized by Alz 50, the chymotryptic fragments were reactive with all the other tau **antibodies**, and the tryptic fragments were positive with five of the **antibodies** (Tau 14, Tau-1, Ab 636.7, NP14, and Tau 46). The peptide maps of A68 differed from that of tau in the number and the size of the peptide fragments. The differences in biochemical properties of these proteins and the sharing multiple epitopes suggest that A68 is a modified form of tau. The modification in part may be due to phosphorylation, although other changes rendering different isoelectrical properties and susceptibility to proteases need to be considered. The removal of the Alz 50 epitope by a cleavage of a 2-3 kDa fragment which does not contain the most C-terminal epitope (Tau 46) indicates that the Alz 50 epitope is located at the N-terminal periphery of the A68 molecule.

L4 ANSWER 16 OF 17 MEDLINE
ACCESSION NUMBER: 85182736 MEDLINE
DOCUMENT NUMBER: 85182736 PubMed ID: 3988771
TITLE: The type 5, acid phosphatase from spleen of humans with hairy cell leukemia. Purification, properties, immunological characterization, and comparison with porcine uteroferrin.
AUTHOR: Ketcham C M; Baumbach G A; Bazer F W; Roberts R M
CONTRACT NUMBER: HD-08560 (NICHD)
T32 CA09126 (NCI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1985 May 10)** 260 (9) 5768-76.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198506
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19850613

AB The spleens of patients with hairy cell leukemia contain high levels of a tartrate-insensitive, cationic, acid phosphatase (the human Type 5 isozyme). This phosphatase has been purified by a procedure which involves only two chromatographic steps: CM-cellulose chromatography and immunoaffinity chromatography on sheep **antibodies** generated against porcine uteroferrin. Uteroferrin is an abundant iron-containing acid phosphatase that can be recovered readily from porcine uterine secretions. Like uteroferrin, the purified human Type **5 phosphatase** is a glycoprotein of molecular weight about 34,000. It contains two atoms of iron/molecule. The human phosphatase and uteroferrin also resemble each other closely in electrophoretic mobility, substrate specificity, and response to a variety of activators and inhibitors. Mouse monoclonal **antibodies** have been raised to uteroferrin and to the human Type **5 phosphatase**. Three monoclonal **antibodies** which bind with high affinities to distinct sites on the uteroferrin molecule also recognize the human spleen enzyme, but bind to it with much lower affinity. These **antibodies** also recognize cationic acid phosphatases purified from bovine and rat spleens. A monoclonal **antibody** raised against the human enzyme, but selected for binding to uteroferrin, appears to recognize a relatively conserved site on all four phosphatases. We conclude that the human Type 5 isozyme belongs to a growing class of structurally related, iron-containing acid phosphatases which includes the iron-transport protein, uteroferrin.

L4 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:119025 CAPLUS
DOCUMENT NUMBER: 114:119025
TITLE: Inositol 1,4,5-trisphosphate 3-kinase distribution in the rat brain. High levels in the hippocampal CA1 pyramidal and cerebellar Purkinje cells suggest its involvement in some memory processes
AUTHOR(S): Mailleux, P.; Takazawa, K.; Erneux, C.; Vanderhaeghen,

J. J.
CORPORATE SOURCE: Lab. Neuropathol. Neuropept. Res., Erasme Acad. Hosp.,
Brussels, Belg.
SOURCE: Brain Research (**1991**), 539(2), 203-10
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The distribution of inositol 1,4,5-triphosphate (InsP3) 3-kinase was studied in the adult rat brain, using **polyclonal antibodies** raised against the purified 50,000-Da rat brain enzyme by immunohistochem. and Western blot, in addn. to enzymic assay. Immunohistochem., the enzyme was detected in neurons, where it was localized in the dendrites and at the periphery of the cell bodies. Using selective toxin lesions, the highest enzyme levels were found in the dendrites of hippocampal CA1 pyramidal cells and in neurons in the dorsal portion of the lateral septum, regions both involved in long-term potentiation; and in the dendrites of Purkinje cell subpopulations in the cerebellum, a region involved in long-term depression. High levels were found in neurons in the cortex, the anterior olfactory nucleus, the striatum (caudate, putamen, olfactory tubercle, Calleja islets, and accumbens), the central nucleus of the amygdala, the hippocampal dentate gyrus, and the subiculum. The enzyme was not detected in other brain regions. By Western blot, a 50,000-Da immunoreactive band was present in the cortex, caudate-putamen and cerebellum. This band was most highly stained in the hippocampus. InsP3 3-kinase activity, stimulated by calcium/calmodulin, corresponded to 6172 pmol of InsP4 produced/min/mg protein in the hippocampus followed by frontal and parietotemporal cortex and cerebellum. This activity was below 400 in the brain stem and spinal cord. Taking into account the possibility of InsP3 3-kinase isoenzymes not recognized by the **antibody**, the existence of the highest InsP3 **5-phosphatase** activity in the cerebellum and the heterogeneity of the enzyme cellular distribution, the immunohistochem. results corresponded reasonably well to the Western blot and enzymic assay.

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| L2 | Nussbaum-R$-l.in. | 3 | L2 |
| L1 | 5-phosphatase | 78 | L1 |

END OF SEARCH HISTORY

72452

**Delaval, Jan**

**From:** Roark, Jessica
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